UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,632	11/13/2003	Lawrence M. Kauvar	388512011000	2417

25225 7590 04/24/2008
MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
04/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/713,632	**Applicant(s)** KAUVAR ET AL.	
	Examiner AMANDA SHAW	**Art Unit** 1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 April 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *3*.
   Claim(s) rejected: *1-17*.
   Claim(s) withdrawn from consideration: *none*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Juliet C Switzer/
Primary Examiner, Art Unit 1634

Continuation of 3. NOTE: The proposed amendment to claim 1 raises the issue of of new matter. In the instant case the claims have been amended to recite "wherein the distance between said probes is as little as 1500 bases". It is noted that the phrase "as little as" has not been defined in the specification therefore the phrase has been given its broadest reasonable interpretation. Thus the amended phrase encompasses situations wherein the distance between the first and second probes is between 0-1500 base pairs. The specification (para 32) teaches that the spacing must be sufficient to accommodate the dimension of the beads because the dimensions appear to swell. This recitation does not support situations encompassed by the claims wherein the distance between the first and second probes is for example 1 base pair. Further the specification teaches that if the beads are to be observed independently they should be spaced at least 250 nm (about 735 base pairs) from one another. Again this recitation does not support situations encompassed by the claims wherein the distance between the first and second probes is for example less than 735 base pairs. While the specification further teaches that analogous calculations can be made depending on the diameter of the beads used for labeling and the magnitude of the apparent swelling the specification does not provide clear support for claimed range which is less than 1500 base pairs.

Additionally the claims have been amended to recite "wherein each of said first and second particulate labels contains at least two fluorophores that emit light of different wavelengths". This phrase brings up issues under 35 USC 112 2nd paragraph because it is unclear if the both the first and second particulate labels contain at least two fluorophores that emit light of different wavelengths or if this recitation means that the first particulate label contains one fluorophore and the second particulate label contains a different fluorophore wherein the fluorophores are different because they emit length of different wavelengths.

As such the proposed amendments are not being entered because further search and consideration would be required. As a result the proposed amendments do not place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

Continuation of 11. does NOT place the application in condition for allowance because: With regard to the rejection made under 35 USC 112 1st paragraph the Applicants arguments pertain to the claims as amended. These arguments are considered moot in view of the non entry of the after final amendment.

With regard to the rejections made under 35 USC 112 2nd paragraph the Applicants arguments pertain to the amended claims. Arguments are addressed only in so far as they are relevent to the claims that were previously examined.

With regard to the rejections made under 35 USC 102 the Applicants arugments pertain to both the pending claims and the amended claims.

The Applicants first argument is based on the limitations of claim 2 that have been incorporated into claim 1. Since this argument pertains only to the amended claims it is considered moot in view of the non entry of the after final amendment.

The Applicants next argument is that there is no separate step in Cai of interrogating a region that has been identified using two separate labels. In the instant case the specification does not define "interrogating" therefore the phrase is given its broadest reasonable interpretation. As such the binding of the labels themselves in Cai has been broadly interpretated as a step of interrogation.

Additionally the Applicants argue that Cai fails to teach a pair of first and second particulated labels that are detected as separate points in space because Cai. Specifically they argue that Cai uses an ultra sensitive luminescence confocal microscope wherein light generated by more than on probe is collected as a single beam and then subsequently split into its component wavelength. Therefore the Applicants believe that this is not the same as observing the presence or absence of each member of any pair as separate points in space. This argument has been fully considered but is not persuasive. Cai teaches a method wherein target sites on a segment of nucleic acid are labeled with separate distinguishable luminescent hybridization probes. Cai further teaches that the target sites are approximately 40 bp apart from one another. The Applicants keep arguing that the probes of Cai are not seen as "separate points in space". However since the Applicants have not provided a fixed definition for what it means to be seen as "separate points in space" this phrase has been broadly interpreted. In the instant case the labels of Cai are being interpreted as being "separate points in space" because they are approximately 40 bp apart from one another. Dectecting both labels inherently results in detection at spearte points in space. Further the claims merely require being able to observe the presence or absence of each label at separate points in space. The method of Cai clearly accomplishes observing the presence or absence of each label even though light generated by more than one probe is collected as a single beam and then subsequently spit into its component wavelengths. In view of the "comprising" language the claims allow for such a step to be performed. The Applicants then argue that Cai teaches away from observing these as single points in space since there is no need to identify a region which is then going to be interrogated however there . They further state that what Cai is doing is not identifying a region but detecting the binding of multiple probes to the same nucleic acid wherein the detection does not identify them in space individually but registers their presence by detecting the presence of the signal from each of them in a single emitted light beam. This argument has been considered but is not fully persuasive. By detecting the binding of multiple probes Cai is identifying a region (the region that the probes hybridized to). As explained above the detection does identify the probes in space individually because each probe has a different label and each probe binds approximately 40 bp from one another. Although the probes are initially detected as a single emitted light beam each individual probes is detected when the light beam is split into its component wavelengths. As such the rejection over Cai is maintained.

With regard to the rejection made under 35 USC 103 the Applicants arguments pertain to both the pending claims and the amended claims. The Applicants first argument is that it makes no sense to use the combinatorial beads of Kauvar in the Cai approach because it would complicate the assay and render it hopelessly cumbersome. This argument has been considered but is not persuasive because this is not the test for obviousness. Further this appears to only be the opinion of the Applciants since they have not provided any evidence to support this. Next the Applicants discuss rejections made over other claims which they indicate recite features that are not necessary for patentability.

Further the conclusion paragraph in the response states that the probes are no seen as separate points in space because the confocal microscopy techinque of Cai detects a single light beam from a DNA molecule containing one or more probes and then subsequently splits this into components. However this would result in observing different labels which are present and the labels themselves are inherently at different points in space. Next the applicants argue that all Cai wants to know is which probes do and do not bind to the target whereas the Applicants method requires both identifying a region and then further interogating the region. However this feature is not claimed because the comprising language of the claims allows for the steps to be performed in any order. Finally the claims have been amended to require the use of combinatorial beads as labels however the amendment has not been entered. For the reasons stated herein these rejections are maintained.